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NEWS 4	AUG 11	STN AnaVist workshops to be held in North America
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NEWS 7	SEP 09	ACD predicted properties enhanced in REGISTRY/ZREGISTRY
NEWS 8	OCT 03	MATHDI removed from STN
NEWS 9	OCT 04	CA/CAplus-Canadian Intellectual Property Office (CIPO) added to core patent offices
NEWS 10	OCT 06	STN AnaVist workshops to be held in North America

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NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
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FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 15:23:31 ON 07 OCT 2005
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http://www.cas.org/ONLINE/DBSS/registryss.html

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                                              ENTRY    SESSION
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FILE LAST UPDATED: 6 Oct 2005  (20051006/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s human () peroxisome () proliferator () activator () receptor or PPAR?
       1490817 HUMAN
        329988 HUMANS
       1654865 HUMAN
                 (HUMAN OR HUMANS)
         14264 PEROXISOME
          4770 PEROXISOMES
         15277 PEROXISOME
                 (PEROXISOME OR PEROXISOMES)
          8601 PROLIFERATOR
          1573 PROLIFERATORS
```

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          9050 PROLIFERATOR
                 (PROLIFERATOR OR PROLIFERATORS)
         94973 ACTIVATOR
         30153 ACTIVATORS
        113438 ACTIVATOR
                 (ACTIVATOR OR ACTIVATORS)
        620601 RECEPTOR
        569476 RECEPTORS
        738707 RECEPTOR
                 (RECEPTOR OR RECEPTORS)
             1 HUMAN (W) PEROXISOME (W) PROLIFERATOR (W) ACTIVATOR (W) RECEPTOR
          6867 PPAR?
L1        6868 HUMAN (W) PEROXISOME (W) PROLIFERATOR (W) ACTIVATOR (W) RECEPTOR
                OR PPAR?

=> s heart () failure?
        311918 HEART
         26848 HEARTS
        313632 HEART
                 (HEART OR HEARTS)
        181940 FAILURE?
L2       18302 HEART (W) FAILURE?

=> s l2 () l1
L3           0 L2 (W) L1

=> s l2 and l1
L4          63 L2 AND L1

=> s l4 and death?
        133892 DEATH?
L5           1 L4 AND DEATH?

=> s l4 and review/dt
       1860854 REVIEW/DT
L6          28 L4 AND REVIEW/DT

=> d l6, ibib abs, 1-28

L6   ANSWER 1 OF 28  HCAPLUS  COPYRIGHT 2005 ACS on STN
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Full Text | Citing References

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ACCESSION NUMBER:         2005:462476  HCAPLUS
DOCUMENT NUMBER:          143:145569
TITLE:                    Fatty acid oxidation inhibition with PPARα
                          activation for normalizing gene expression in heart
                          failure?
AUTHOR(S):                Rupp, Heinz; Rupp, Thomas P.; Maisch, Bernhard
CORPORATE SOURCE:         Molecular Cardiology Laboratory, Department of
                          Internal Medicine and Cardiology, Philipps University
                          of Marburg, Marburg, 35033, Germany
SOURCE:                   Cardiovascular Research (2005), 66(3), 423-426
                          CODEN: CVREAU; ISSN: 0008-6363
PUBLISHER:                Elsevier B.V.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
AB   A review.  The research of Lionetti et al. (2005) entitled "Carmitine
     palmitoyl transferase-1 inhibition prevents ventricular remodeling and
     delays decompensation in pacing-induced heart failure" is reviewed
     with commentary and refs.  Lionetti et al. provide clear evidence that the
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carnitine palmitoyl transferase 1 inhibitor oxfenicine slowed progression of **heart failure** and preserved pump function.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:347723 HCAPLUS
DOCUMENT NUMBER: 142:456161
TITLE: Metabolism and the hypertrophied heart of the elderly. A target for the drug group "fatty acid oxidation inhibitors with **PPAR**α activation"?
AUTHOR(S): Rupp, H.; Rupp, T. P.; Maisch, B.
CORPORATE SOURCE: Molekular-kardiologisches Labor, Klinik fuer Innere Medizin und Kardiologie, Philipps-Universitaet, Marburg, Germany
SOURCE: Deutsche Medizinische Wochenschrift (2005), 130(12), 726-730
CODEN: DMWOAX; ISSN: 0012-0472
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: German

AB A review. Metabolic changes in the hypertrophied hearts of elderly are discussed, the influence of age, blood hypertension, and diabetes mellitus on it, and pharmacol. therapies with e.g. clofibrate and etomoxir. A focus is on function, effects, and changes of the transcription factor peroxisome proliferator-activated receptor α.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:246975 HCAPLUS
DOCUMENT NUMBER: 142:277505
TITLE: Peroxisome proliferator-activated receptors and cardiovascular remodeling
AUTHOR(S): Schiffrin, Ernesto L.
CORPORATE SOURCE: Canadian Institute of Health Research Multidisciplinary Research Group on Hypertension, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: American Journal of Physiology (2005), 288(3, Pt. 2), H1037-H1043
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Peroxisome proliferator-activated receptors (**PPARs**) are nuclear receptors that heterodimerize with the retinoid X receptor and then modulate the function of many target genes. Three **PPARs** are known: α, β/δ, and γ. The better known are **PPAR**-α and **PPAR**-γ, which may be activated by different synthetic agonists, although the endogenous ligands are unknown. **PPAR**-α is involved in fatty acid oxidn. and expressed in the liver, kidney, and skeletal muscle, whereas **PPAR**-γ is involved in fat cell differentiation, lipid storage, and insulin sensitivity. However, both have been shown to be present in variable amts. in cardiovascular tissues,

including endothelium, smooth muscle cells, macrophages, and the heart. The activators of **PPAR**-α (fibrates) and **PPAR**-γ (thiazolidinediones or glitazones) antagonized the actions of angiotensin II in vivo and in vitro and exerted cardiovascular antioxidant and anti-inflammatory effects. **PPAR** activators lowered blood pressure, induced favorable effects on the heart, and cor. vascular structure and endothelial dysfunction in several rodent models of hypertension. Activators of **PPARs** may become therapeutic agents useful in the prevention of cardiovascular disease beyond their effects on carbohydrate and lipid metab. Some side effects, such as wt. gain, as well as documented aggravation of advanced **heart failure** through fluid retention by glitazones, may, however, limit their therapeutic application in prevention of cardiovascular disease.

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Full Text | Citing References

ACCESSION NUMBER: 2005:126198 HCAPLUS
DOCUMENT NUMBER: 142:441036
TITLE: Thiazolidinediones: a review of their mechanisms of insulin sensitization, therapeutic potential, clinical efficacy, and tolerability
AUTHOR(S): Vasudevan, Abu R.; Balasubramanyam, Ashok
CORPORATE SOURCE: Division of Diabetes, Endocrinology, and Metabolism, Baylor College of Medicine, Houston, TX, USA
SOURCE: Diabetes Technology & Therapeutics (2004), 6(6), 850-863
CODEN: DTTHFH; ISSN: 1520-9156
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The thiazolidinediones (TZDs) rosiglitazone and pioglitazone are newer addns. to the antidiabetic armamentarium and are indicated for the treatment of type 2 diabetes mellitus (T2DM) in the United States. The TZDs are peroxisome proliferator-activated receptor-γ (**PPAR**-γ) agonists that provide clin. effective glycemic control and unique pharmacol. effects on multiple risk factors for T2DM-related morbidity, including improvement of insulin sensitivity and endothelial dysfunction, redn. of blood pressure, and amelioration of dyslipidemia. Wt. gain and fluid retention occur with TZD therapy, esp. when they are administered in higher doses and in combination with insulin. Although fluid retention assocd. with the use of TZDs is generally mild and reversible, these agents should not be used in patients with New York Heart Assocn. Class III or IV **heart failure** symptoms. The findings of ongoing, long-term, prospective studies will clarify the role of the TZDs in the treatment of T2DM, particularly in terms of the durability of improvements in glycemic control, insulin sensitivity, pancreatic β-cell function, and cardiovascular health.

REFERENCE COUNT: 137 THERE ARE 137 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:104456 HCAPLUS
DOCUMENT NUMBER: 143:52583

TITLE: Renin-angiotensin system inhibition prevents type 2 diabetes mellitus: Part 2. Overview of physiological and biochemical mechanisms
AUTHOR(S): Scheen, A. J.
CORPORATE SOURCE: Division of Diabetes, Nutrition and Metabolic Disorders, Department of Medicine, CHU Sart Tilman, Liege, Belg.
SOURCE: Diabetes & Metabolism (2004), 30(6), 498-505
CODEN: DIMEFW; ISSN: 1262-3636
PUBLISHER: Masson Editeur
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The inhibition of the renin-angiotensin system (RAS) with either angiotensin converting enzyme inhibitors (ACEIs) or AT1 angiotensin receptor blockers (ARBs) consistently and significantly reduces the incidence of type 2 diabetes in patients with hypertension or congestive **heart failure**. The mechanisms underlying this protective effect appear to be complex and may involve an improvement of both insulin sensitivity and insulin secretion. These two effects may result, at least in part, from the well known effects of these pharmacol. agents on the vascular system on the one hand, on the ionic balance on the other hand. Indeed, the vasodilation induced by ACEIs or ARBs could improve the blood circulation in skeletal muscles, thus favoring peripheral insulin action, but also in the pancreas, thus promoting insulin secretion. Preserving cellular potassium and magnesium pools by blocking the aldosterone effects could also improve both cellular insulin action and insulin secretion. However, besides these classical effects, new mechanisms have been recently suggested. A direct effect of the inhibition of angiotensin and/or of the enhancement of bradykinin on various steps of the insulin cascade signalling has been described as well an increase in GLUT4 glucose transporters after RAS inhibition. Furthermore, it has been demonstrated that angiotensin II inhibits adipogenic differentiation of human adipocytes via A1 receptors and, therefore, it has been hypothesised that RAS blockade may prevent diabetes by promoting the recruitment and differentiation of adipocytes. Finally, some lipophilic ARBs appear to induce **PPAR**-gamma activity in the adipose tissue. Hence, the protection against type 2 diabetes obsd. after RAS inhibition may be partially linked to a thiazolidinedione-like effect. In conclusion, numerous physiol. and biochem. mechanisms could explain the protective effect of RAS inhibition against the development of type 2 diabetes in individuals with arterial hypertension or congestive **heart failure**. What might be the main mechanism in the overall protection effect of ACEIs or ARBs remains an open question.

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2005:87156 HCAPLUS
DOCUMENT NUMBER: 142:347822
TITLE: Peroxisome proliferator-activated receptor α and hypertensive heart disease
AUTHOR(S): Goikoetxea, Maria J.; Beaumont, Javier; Diez, Javier
CORPORATE SOURCE: Area of Cardiovascular Pathophysiology, Centre for Applied Medical Research, University Clinic, School of Medicine, University of Navarra, Pamplona, Spain
SOURCE: Drugs (2004), 64(Suppl. 2), 9-18
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Peroxisome proliferator-activated receptor α (**PPARα**) is a ligand-activated transcription factor belonging to the nuclear hormone receptor superfamily. It is expressed by cardiomyocytes and regulates gene expression of key proteins involved in myocardial lipid and energy metab. Accordingly, the activity of **PPARα** is an important determinant of cardiomyocyte lipid homeostasis and ATP prodn. Currently, animal and human data suggest that deactivation of **PPARα** may contribute substantially to phenotypic changes that accompany cardiac growth in conditions of pressure overload, and the hypothesis emerges that a compromised **PPARα** activity may participate in the transition from compensated left ventricular hypertrophy to **heart failure** in hypertensive heart disease. The availability of **PPARα** activators (e.g. fibric acid derivates and statins) must stimulate investigation into the potential cardioprotective actions of these compds. beyond their hypolipidemic effects and via restoration of **PPARα** activity in the hypertrophied and failing heart.

REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:1020283 HCAPLUS
DOCUMENT NUMBER: 142:195105
TITLE: The pathophysiologic mechanism of **PPARγ** and its activators on ventricular remodeling and **heart failure**
AUTHOR(S): Zhao, Ying
CORPORATE SOURCE: General Hospital of PLA, Beijing, 100853, Peop. Rep. China
SOURCE: Wujing Yixueyuan Xuebao (2004), 13(4), 333-335
CODEN: WYXUA9; ISSN: 1008-5041
PUBLISHER: Wujing Yixueyuan Xuebao Bianjibu
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Chinese

AB A review. Topics discussed include: general description of Peroxisome proliferator-activated receptor γ (**PPARγ**); effects of **PPARγ** in **heart failure** and ventricular remodeling; significance of clin. application of **PPARγ** and limitations.

L6 ANSWER 8 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:954013 HCAPLUS
DOCUMENT NUMBER: 142:68390
TITLE: Mitochondrial Dysfunction by Synthetic Ligands of Peroxisome Proliferator Activated Receptors (**PPARs**)
AUTHOR(S): Scatena, Roberto; Martorana, Giuseppe; Bottoni, Patrizia; Giardina, Bruno
CORPORATE SOURCE: Istituto di Biochimica e Biochimica Clinica, Universita Cattolica del Sacro Cuore, Rome, 00168, Italy
SOURCE: IUBMB Life (2004), 56(8), 477-482
CODEN: IULIF8; ISSN: 1521-6543
PUBLISHER: Taylor & Francis Ltd.

DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. **PPARs** are a class of nuclear receptors involved in lipid and glucidic metab., immune regulation and cell differentiation. This spectrum of biol. activities stimulated pharmacol. research to synthesize different mols. with **PPARs** binding activity with beneficial therapeutic effects. As a matter of fact, some synthetic **PPAR**-ligands were already employed in pharmacotherapy: **PPAR**-α ligands, such as fibrates, are used in hyperlipidemias and thiazolidinediones, mainly **PPAR**-γ ligands, are employed as insulin sensitizers. However, both classes of drugs showed pharmacotoxicol. profiles which cannot be fully ascribed to activation of their specific receptors and which are causing a growing incidence of dramatic side effects (rhabdomyolysis, acute liver failure, **heart failure**, etc.). A re-evaluation of the biol. activities of **PPAR** synthetic ligands, in particular of the mitochondrial dysfunction based on a rotenone-like Complex I partial inhibition and of its consequent metabolic adaptations, seems to explain some of the pathophysiol. aspects of **PPARs** allowing a better definition of the therapeutic properties of the so-called **PPAR**-ligands.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2004:939478 HCAPLUS
DOCUMENT NUMBER: 142:232129
TITLE: Combined thiazolidinedione-insulin therapy: Should we be concerned about safety?
AUTHOR(S): Scheen, Andre J.
CORPORATE SOURCE: Division of Diabetes, Nutrition and Metabolic Disorders, Department of Medicine, CHU Sart Tilman, Liege, Belg.
SOURCE: Drug Safety (2004), 27(12), 841-856
CODEN: DRSAEA; ISSN: 0114-5916
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Thiazolidinediones, also called glitazones, are insulin sensitizers that act as agonists of the peroxisome proliferator-activated receptors-gamma (**PPAR**γ). After the withdrawal of troglitazone due to hepatotoxicity, only pioglitazone and rosiglitazone can be used for treating patients with type 2 diabetes mellitus, either as monotherapy or in combination with metformin or with sulfonylureas (or glinides). The combination of glitazones with insulin is also appealing, as it allows improvement of glycemic control while decreasing the daily insulin requirement. Insulin dosage has to be adjusted regularly to avoid hypoglycemic episodes. However, some concerns have been raised about such combined glitazone-insulin therapy because it may favor wt. gain due to both enhanced adipogenesis and fluid retention. Such adverse effects are commonly obsd. in all diabetic individuals receiving glitazones, whatever the mode of use, but they appear to be exacerbated in insulin-treated patients. Body fat gain is a major drawback of treatment with adipogenic compds. such as glitazones. However, some evidence suggests that the fat is redistributed in a favorable direction, i.e., from visceral to s.c. depots, although no long-term follow-up is yet available. An estd. 2-5% of patients receiving glitazone monotherapy and 5-15% receiving concomitant insulin therapy experience peripheral edema. Some anecdotal cases of pulmonary edema have also been reported, esp. in insulin-treated

patients, although the actual incidence of this complication is unknown. All glitazones increase the intravascular vol. by approx. 6-7% in a dose-dependent manner. Rather than a direct effect on cardiac or renal function, fluid retention and tissue edema seem to be part of a vascular 'leak' syndrome. Such a phenomenon may have greater consequences in patients with type 2 diabetes treated with insulin because such patients are usually older, have had the disease long-term and have worse cardiac or renal function. Addnl., glitazones may potentiate the renal effects of insulin on sodium and water retention. Regardless of the mechanism, it is conceivable that addnl. fluid retention caused by glitazones may alter the already precarious vol. status in patients with underlying cardiac or renal dysfunction, thus leading to edema and congestive **heart failure**. Thus, it is prudent to either avoid glitazones or use them cautiously in individuals with impaired cardiac function. Further studies are clearly needed to define the mechanisms of fluid retention assocd. with glitazone use and to det. the safety of cautious use of these new insulin sensitizers in insulin-treated patients with type 2 diabetes.

REFERENCE COUNT: 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:784232 HCAPLUS
DOCUMENT NUMBER: 142:211096
TITLE: Drug development based on functional genomics of overloaded cardiomyocytes: carnitine palmitoyltransferase 1 vs. **PPAR** alpha effects of etomoxir
AUTHOR(S): Rupp, Heinz; Zarain-Herzberg, Angel; Maisch, Bernhard
CORPORATE SOURCE: Molecular Cardiology Laboratory, Department of Internal Medicine and Cardiology, Philipps University of Marburg, Marburg, Germany
SOURCE: Progress in Experimental Cardiology (2003), 9(Frontiers in Cardiovascular Health), 177-194
CODEN: PEXCFF; ISSN: 1389-1774
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. The review discusses possible drug targets for therapy of **heart failure** and effectiveness of etomoxir.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:784213 HCAPLUS
DOCUMENT NUMBER: 141:409083
TITLE: Inflammation and cardiovascular disease
AUTHOR(S): Willerson, James T.
CORPORATE SOURCE: Texas Heart Institute, St. Luke's Episcopal Hospital, University of Texas Health Science Center at Houston, Houston, TX, USA
SOURCE: Progress in Experimental Cardiology (2003), 9(Frontiers in Cardiovascular Health), 3-18
CODEN: PEXCFF; ISSN: 1389-1774
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review. The role of inflammation in initiating and sustaining various cardiovascular problems, including the conversion from stable to unstable coronary heart disease syndromes, vascular aneurysms, and congestive **heart failure** is reviewed. Various interventions that reduce inflammation in the coronary arteries and hearts in humans, including marked lipid lowering, wt. loss, Peroxisome Proliferator Activated Receptors agonists (**PPAR**), aspirin, and monoclonal antibodies to vascular cell adhesion mol. (VCAM) and intercellular vascular adhesion mol. (ICAM) are identified. Whereas estrogens may promote increases in vascular markers suggesting the presence of inflammation, recent evidence suggests that combined estrogen and progesterone in postmenopausal women may reduce the vascular markers of inflammation. However, the combination of estrogens and progesterone may actually increase the risk of vascular events in menopausal women with cardiovascular disease. Addnl. work is needed to identify the best ways to prevent and/or modulate vascular and myocardial inflammation with the expectation that from these interventions will cone the ability to treat more effectively and perhaps retard the development of atherosclerosis, **heart failure** and vascular aneurysms. Inflammation plays a major role in initiating and sustaining cardiovascular problems, including the conversion from stable to unstable coronary heart disease syndromes, the development of vascular aneurysms, and congestive **heart failure** (1-5). The presence of inflammation also serves as an important predictor of fixture adverse events following interventional procedures in coronary arteries (6). However, inflammation may also serve to identify the presence of unstable or vulnerable atherosclerotic plaques potentially allowing their treatment prior to their fissuring or ulceration and otherwise causing unstable angina and acute myocardial infarction (7,8). In this chapter, potential mechanisms responsible for vascular and myocardial inflammation, consequences of such inflammation, systemic markers identifying the presence of inflammation, and potential treatments of cardiovascular inflammation are discussed.

REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Cited References

ACCESSION NUMBER: 2004:644520 HCAPLUS

DOCUMENT NUMBER: 141:184468

TITLE: Pleiotropic actions of **PPAR**γ activators thiazolidinediones in cardiovascular diseases

AUTHOR(S): Takano, Hiroyuki; Hasegawa, Hiroshi; Zou, Yunzeng; Komuro, Issei

CORPORATE SOURCE: Department of Cardiovascular Science and Medicine, Chiba University Graduate School of Medicine, Chiba, 260-8670, Japan

SOURCE: Current Pharmaceutical Design (2004), 10(22), 2779-2786
CODEN: CPDEFP; ISSN: 1381-6128

PUBLISHER: Bentham Science Publishers Ltd.

DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review. Peroxisome proliferator-activated receptors (**PPARs**) are transcription factors belonging to the nuclear receptor superfamily and form heterodimers with retinoid X receptor. To date, 3 **PPARs** isoforms were isolated and termed α, β (or δ), and γ.

Although **PPAR**γ is expressed predominantly in adipose tissue and assocd. with adipocyte differentiation and glucose homeostasis, it was

recently demonstrated that **PPARγ** is present in a variety of cell types. Synthetic antidiabetic thiazolidinediones (TZDs) and natural prostaglandin D2 (PGD2) metabolite, 15-deoxy-Δ12, 14-prostaglandin J2 (15d-PGJ2), are well-known as ligands for **PPARγ**. After it was reported that activation of **PPARγ** suppresses prodn. of pro-inflammatory cytokines in activated macrophages, medical interest in **PPARγ** have grown and a huge research effort was concd. **PPARγ**, is currently known to be implicated in various human chronic diseases such as diabetes mellitus, atherosclerosis, rheumatoid arthritis, inflammatory bowel disease, and Alzheimer's disease. Moreover, **PPARγ** ligands have potent tumor modulatory effects against colorectal, prostate, and breast cancers. Recent studies suggest that TZDs not only ameliorate insulin sensitivity but also have pleiotropic effects on many tissues and cell types. Although activation of **PPARγ** seems to have beneficial effects on atherosclerosis and **heart failure**, the mechanisms by which **PPARγ** ligands prevent the development of cardiovascular diseases are not fully understood. This review will focus on the latest developments in the **PPARγ** field and the roles of **PPARγ**-dependent pathway in cardiovascular diseases.

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:638590 HCAPLUS
DOCUMENT NUMBER: 142:168534
TITLE: Ligands of the peroxisome proliferator-activated receptor-γ and **heart failure**. [Erratum to document cited in CA140:314230]
AUTHOR(S): Thiemermann, Christoph
CORPORATE SOURCE: The Department of Experimental Medicine, Nephrology and Critical Care, William Harvey Research Institute, St Bartholomew's and The Royal London School of Medicine and Dentistry, London, EC1M 6BQ, UK
SOURCE: British Journal of Pharmacology (2004), 142(6), 1049-1051
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. The cor. version of the paper is given.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:204417 HCAPLUS
DOCUMENT NUMBER: 141:347156
TITLE: Mechanism of regulation of myocardial energy metabolism by peroxisome proliferator activated receptor
AUTHOR(S): Ye, Ping
CORPORATE SOURCE: Department of Geratic Cardiology, General Hospital of PLA, Beijing, 100853, Peop. Rep. China
SOURCE: Zhongguo Dongmai Yinghua Zazhi (2003), 11(1), 81-83
CODEN: ZDYZFM; ISSN: 1007-3949

PUBLISHER: Zhongguo Dongmai Yinghua Zazhi Bianjibu
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Chinese
AB A review on the important role of **PPAR** in regulation of myocardial energy metab., change of activity of **PPAR** in hypertrophied and failing heart, and the effect of **PPAR** γ on hypertrophied and ischemia-reperfusion injury.

L6 ANSWER 15 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2004:152677 HCAPLUS
DOCUMENT NUMBER: 140:314230
TITLE: Ligands of the peroxisome proliferator-activated receptor-γ and **heart failure**
AUTHOR(S): Thiemermann, C.
CORPORATE SOURCE: The Department of Experimental Medicine, Nephrology and Critical Care, William Harvey Research Institute, St Bartholomew's and The Royal London School of Medicine and Dentistry, London, EC1M 6BQ, UK
SOURCE: British Journal of Pharmacology (2004), 141(1), 1-3
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Peroxisome proliferator-activated receptors (**PPARs**) are members of the nuclear hormone receptor superfamily of ligand-activated transcription factors that are related to retinoid, steroid and thyroid hormone receptors. The **PPAR** subfamily comprises of three members, **PPAR**-α, **PPAR**-β and **PPAR**-γ. There is good evidence that ligands of **PPAR**-γ, including certain thiazolinediones, reduce myocardial tissue injury and infarct size. The use of **PPAR**-γ agonists in the treatment of **heart failure** is, however, controversial.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References
ACCESSION NUMBER: 2004:147833 HCAPLUS
DOCUMENT NUMBER: 141:184358
TITLE: Preservation of left ventricular function following ischemia-reperfusion by peroxisome-proliferator activated receptor-gamma (**PPAR**-γ) ligands
AUTHOR(S): Molavi, B.; Rasouli, N.; Chen, H.; Mehta, J. L.
CORPORATE SOURCE: Department of Internal Medicine, Physiology and Biophysics, University of Arkansas and Central Arkansas Veterans Healthcare System, Little Rock, AR, USA
SOURCE: Advances in Heart Failure, Proceedings of the World Congress on Heart Failure: Mechanisms and Management, 8th, Washington, DC, United States (2002), 3-11.
Editor(s): Kimchi, Asher. Medimond: Bologna, Italy.
CODEN: 69FBTG; ISBN: 88-323-2713-9
DOCUMENT TYPE: Conference; **General Review**
LANGUAGE: English
AB A review. Tissue injury following ischemia-reperfusion is a well-described pathophysiol. process that is defined as exacerbation of the hypoxic injury following restoration of oxygenation to the ischemic

tissue. The phenomenon of reperfusion injury is encountered in a variety of common clin. and lab. settings including acute myocardial infarction, tissue transplant and coronary artery bypass grafting. Although the precise mechanism of reperfusion injury is not clear, there is mounting evidence that release of free radicals, complement activation and an intense post-reperfusion inflammatory response participate in its genesis. Cardiac manifestations of reperfusion injury include deterioration of left ventricular systolic and diastolic function resulting in **heart failure**, and cardiac arrhythmias (1). Several strategies that scavenge free radicals and decrease the ensuing inflammatory reactions and complement activation have been examd. There has recently been a surge of interest in **PPAR**-γ ligands in the therapy of reperfusion injury due to potent "anti-oxidant" and "anti-inflammatory" effects of these agents. This review summarizes these recent advances.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:145273 HCAPLUS
DOCUMENT NUMBER: 141:166963
TITLE: Cardioprotective effects of thiazolidinediones, peroxisome proliferator-activated receptor-γ agonists
AUTHOR(S): Yue, Tian-Li
CORPORATE SOURCE: Department of Investigative and Cardiac Biology, GlaxoSmithKline Pharmaceuticals, King of Prussia, PA, USA
SOURCE: Drugs of Today (2003), 39(12), 949-960
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Greater myocardial injury in response to ischemia/reperfusion (I/R) and increased incidence of congestive **heart failure** and death in noninsulin-dependent diabetes mellitus, or type 2 diabetes, patients has been clearly identified. Thiazolidinediones (TZDs), peroxisome proliferator-activated receptor-γ (**PPAR**-γ) agonists, act as insulin sensitizers and are a novel class of oral antidiabetic drugs. An emerging body of evidence, mainly from preclin. studies, suggest that TZDs protect the heart from acute I/R injury and also might attenuate cardiac remodeling and **heart failure**. The mechanisms involved in this cardioprotection by TZDs are multifactorial and not completely understood. These novel activities of TZDs could benefit type 2 diabetes patients and offer benefits beyond glycemic control. This new knowledge about the cardioprotective effects of TZDs is still limited, and more investigations, esp. clin. studies, are required.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2004:58260 HCAPLUS
DOCUMENT NUMBER: 141:120927
TITLE: Relationship between vascular failure and inflammation
AUTHOR(S): Node, Koichi
CORPORATE SOURCE: School of Medicine, Dep. of Circulatory Diseases, Saga University, Japan

SOURCE: Igaku to Yakugaku (2003), 50(4), 449-469
CODEN: IGYAEI; ISSN: 0389-3898
PUBLISHER: Shizen Kagakusha
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Japanese
AB A review. The topics discussed are (1) inflammation in acute coronary syndrome; (2) relationships among oxidative stress, endothelial dysfunction, unstable plaque rapture and cardiac infarction; (3) vascular failure and **heart failure**; (4) statin effects in patients with **heart failure**; (5) mol. mechanisms of vascular dilation by nitric oxide (NO) and epoxyeicosatrienoic acid (EET); (6) EETs as ligands for **PPAR**; (7) endothelial dysfunction and reduced vascular dilation in diabetes; (8) eNOS and CYP2J2 gene polymorphisms in hyperinsulinemia and diabetes.

L6 ANSWER 19 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2003:654532 HCAPLUS
DOCUMENT NUMBER: 140:70030
TITLE: The role of **PPAR**γ-dependent pathway in the development of cardiac hypertrophy
AUTHOR(S): Takano, Hiroyuki; Hasegawa, Hiroshi; Nagai, Toshio; Komuro, Issei
CORPORATE SOURCE: Department of Cardiovascular Science and Medicine, Chiba University Graduate School of Medicine, Chiba, Japan
SOURCE: Drugs of Today (2003), 39(5), 347-357
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Peroxisome proliferator-activated receptors (**PPARs**) are transcription factors belonging to the nuclear receptor superfamily. **PPARs** have 3 isoforms, α, β (or δ) and γ. It was conceived that **PPAR**γ is expressed predominantly in adipose tissue and promotes adipocyte differentiation and glucose homeostasis. Recently, synthetic antidiabetic thiazolidinediones and natural prostaglandin D2 (PGD2) metabolite, 15-deoxy-Δ12,14-prostaglandin J2 (15d-PGJ2), were identified as ligands for **PPAR**γ. Following demonstration that **PPAR**γ is present in a variety of cell types, further study of **PPAR**γ was conducted. Although activation of **PPAR**γ appears to have beneficial effects on atherosclerosis and **heart failure**, it is still largely uncertain whether **PPAR**γ ligands prevent the development of cardiovascular diseases. Recent evidence suggests that some benefit from the antidiabetic agents known as thiazolidinediones may occur through **PPAR**γ-independent mechanisms. In this review, the authors report on the latest developments concerning the study of **PPARs** and summarize the roles of the **PPAR**γ-dependent pathway in cardiovascular diseases.
REFERENCE COUNT: 99 THERE ARE 99 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN
Full Text | Citing References

ACCESSION NUMBER: 2003:614947 HCAPLUS
DOCUMENT NUMBER: 139:361948
TITLE: Gene regulation of fatty acids oxidation enzymes in

myocardium and the role of **PPARα**
AUTHOR(S): Hu, Qin; Li, Longgui
CORPORATE SOURCE: Department of Cardiology, Xinqiao Hospital, Third Military Medical University, Chungking, 400037, Peop. Rep. China
SOURCE: Zhongguo Bingli Shengli Zazhi (2002), 18(12), 1552-1556
CODEN: ZBSZEB; ISSN: 1000-4718
PUBLISHER: Jinan Daxue
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: Chinese
AB A review. The mammalian fetal heart relies primarily on glucose and pyruvate as substrates for ATP prodn., and it is rapidly transformed to fatty acid 3 - oxidn. (FAO) postnatally. However, energy metabolic pathways revert to a fetal pattern, when cardiac hypertrophy and **heart failure** developed. This return was called recapitulation, ultimately it is maladaptive for the body. The process of FAO was performed under a precise regulating system, nuclear transcription factors such as **PPARα**, Sp1/3, Coup-TF (chicken ovalbumin upstream promoter transcription factor) all take part in the regulation of genes transcription of FAO enzymes. It was identified that the regulation of **PPARα** activity in hypertrophic myocardium due to pressure overload might result in down-regulation of gene expression of FAO enzyme. The mechanism involved in reinduction of a fetal gene transcription participated in the regulation of myocardial energy metab. in the development of cardiac hypertrophy resulting from pressure overload.

L6 ANSWER 21 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2003:66489 HCAPLUS
DOCUMENT NUMBER: 139:20161
TITLE: Role of nitric oxide in matrix remodeling in diabetes and **heart failure**
AUTHOR(S): Tyagi, Suresh C.; Hayden, Melvin R.
CORPORATE SOURCE: Department of Physiology and Biophysics, University of Mississippi Medical Center, Jackson, MS, USA
SOURCE: Heart Failure Reviews (2003), 8(1), 23-28
CODEN: HFREFC; ISSN: 1382-4147
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English
AB A review. Accumulation of oxidized-matrix between the endothelium and myocytes is assocd. with endocardial endothelial (EE) dysfunction in diabetes and **heart failure**. High levels of circulating homocysteine (Hcy) have been demonstrated in diabetes mellitus (DM). These high levels of Hcy (hyperhomocysteinemia, HHcy) have a neg. correlation with peroxisome proliferator activated receptor (**PPAR**) expression. Studies have demonstrated that Hcy decreases bioavailability of endothelial nitric oxide (eNO), generates nitrotyrosine, and activates latent matrix metalloproteinase (MMP), instigating EE dysfunction. **PPAR** ligands ameliorate endothelial dysfunction and DM. In addn. Hcy competes with **PPAR** ligands. The understanding of mol., cellular, and extracellular mechanisms by which Hcy amplifies DM will have therapeutic ramifications for diabetic cardiomyopathy.
REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 22 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:481984 HCAPLUS
DOCUMENT NUMBER: 137:308060
TITLE: Gene Regulatory Mechanisms Governing Energy Metabolism during Cardiac Hypertrophic Growth
AUTHOR(S): Lehman, John J.; Kelly, Daniel P.
CORPORATE SOURCE: Departments of Medicine and Molecular Biology & Pharmacology, Center for Cardiovascular Research, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Heart Failure Reviews (2002), 7(2), 175-185
CODEN: HFREFC; ISSN: 1382-4147
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Studies in a variety of mammalian species, including humans, have demonstrated a redn. in fatty acid oxidn. (FAO) and increased glucose utilization in pathol. cardiac hypertrophy, consistent with reinduction of the fetal energy metabolic program. This review describes results of recent mol. studies aimed at delineating the gene regulatory events which facilitate myocardial energy substrate switches during hypertrophic growth of the heart. Studies aimed at the characterization of transcriptional control mechanisms governing FAO enzyme gene expression in the cardiac myocyte have defined a central role for the fatty acid-activated nuclear receptor peroxisome proliferator-activated receptor α (**PPARα**). Cardiac FAO enzyme gene expression was shown to be coordinately downregulated in murine models of ventricular pressure overload, consistent with the energy substrate switch away from fatty acid utilization in the hypertrophied heart. Nuclear protein levels of **PPARα** decline in the ventricle in response to pressure overload, while several Sp and nuclear receptor transcription factors are induced to fetal levels, consistent with their binding to DNA as transcriptional repressors of rate-limiting FAO enzyme genes with hypertrophy. Knowledge of key components of this transcriptional regulatory pathway will allow for the development of genetic engineering strategies in mice that will modulate fatty acid oxidative flux and assist in defining whether energy metabolic derangements play a primary role in the development of pathol. cardiac hypertrophy and eventual progression to **heart failure**.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:270592 HCAPLUS
DOCUMENT NUMBER: 137:199000
TITLE: Peroxisome proliferator-activated receptor α as a genetic determinant of cardiac hypertrophic growth. Culprit or innocent bystander?
AUTHOR(S): Kelly, Daniel P.
CORPORATE SOURCE: Center for Cardiovascular Res., Depts. of Medicine, Molecular Biology and Pharmacology and Pediatrics, Washington Univ. School of Medicine, St. Louis, MO, USA
SOURCE: Circulation (2002), 105(9), 1025-1027
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**

LANGUAGE: English

AB A review. The study by Jamshidi et al. has identified the human **PPARα** gene as a new candidate genetic modifier of the cardiac hypertrophic response. These results are exciting despite the fact that a cause-effect relationship has not yet been established. A hallmark of an important descriptive study is that it raises more questions than answers. The Jamshidi study meets this criterion. Among the many questions raised by this study are (1) What is the significance of the obsd. sex difference in the assocn. between the **PPARA**-C allele and LVH in hypertensive subjects. As suggested by the authors, it is tempting to speculate that the sex difference relates to the observation that male mice lacking **PPARα** show a more pronounced phenotype than do female mice. (2) Does the **PPARα**-C allele identify individuals with LVH at increased risk for progression to pathol. remodeling and **heart failure**. Jamshidi et all did not address this question. However, thc surprising observation that LV mass was greater in individuals with the **PPARα**-C allele in the context of both physiol. and pathol. hypertrophy indicates that this marker may not be predictive of a pathol. outcome. (3) Is **PPARα** a target for the development of new therapeutic approaches for patients with pathol. forms of LVH at risk for developing **heart failure**. **PPARA** agonists with relatively weak cardiac activity (eg, gemfibrozil) already exist as hypolipidermic agents. However, before evaluation of **PPARα** agonists for use as treatment of patients with pathol. LVH begins, the role of altered **PPARα** activity in the treatment of hypertrophied heart as adaptive or maladaptive must be defined. (4) Are other components of the **PPARα** transcriptional regulatory complex, such as the nuclear receptor RXR, modifiers of the cardiac hypertrophic response. The answers to these questions await future studies as the authors enter a new era of clin. research involving the application of genomics and genotype-phenotype analyses to common cardiovascular diseases.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:214583 HCAPLUS
DOCUMENT NUMBER: 137:56828
TITLE: Therapeutic potential of CPT I inhibitors: cardiac gene transcription as a target
AUTHOR(S): Zarain-Herzberg, Angel; Rupp, Heinz
CORPORATE SOURCE: Laboratorio de Biologia Molecular, Departamento de Bioquimica, Facultad de Medicina, Universidad Nacional Autonoma de Mexico, Mexico, Mex.
SOURCE: Expert Opinion on Investigational Drugs (2002), 11(3), 345-356
CODEN: EOIDER; ISSN: 1354-3784
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Inhibitors of carnitine palmitoyl-transferase I (CPT I), the key enzyme for the transport of long-chain acyl-CoA compds. into mitochondria, have been developed as agents for treating diabetes mellitus Type 2. Findings that the CPT I inhibitor, etomoxir, has effects on overloaded heart muscle, which are assocd. with an improved function, were unexpected and can be attributed to selective changes in the dysregulated gene expression of hypertrophied cardiomyocytes. Also, the first clin. trial with etomoxir in patients with **heart failure** showed that

etomoxir improved the clin. status and several parameters of heart function. In view of the action of etomoxir on gene expression, putative mol. mechanisms involved in an increased expression of SERCA2, the Ca2+ pump of sarcoplasmic reticulum (SR) and α-myosin heavy chain (MHC) of failing overloaded heart muscle are described. The first 225 bp of human, rabbit, rat and mouse SERCA2 promoter sequence have high identity. Various cis-regulatory elements are also given for the promoter of the rat cardiac α-MHC gene. It is hypothesized that etomoxir increases glucose-phosphate intermediates resulting in activation of signaling pathway(s) mediated by phosphatases. Regarding the possible direct action of etomoxir on peroxisome proliferator activated receptor alpha (**PPAR**-α) activation, it could upregulate the expression of various enzymes that participate in beta-oxidn., thereby modulating some effects of CPT 1 inhibition. Any development of alternative drugs requires a better understanding of the signal pathways involved in the altered gene expression. In particular, signals need to be identified which are altered in overloaded hearts and can selectively be re-activated by etomoxir.

REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2002:54330 HCAPLUS
DOCUMENT NUMBER: 137:18311
TITLE: Lipid metabolism in the heart contribution of BMIPP to the diseased heart
AUTHOR(S): Nohara, Ryuji
CORPORATE SOURCE: Department of Medicine, Tazuke Kofukai Medical Research Institute, Osaka, 530-8480, Japan
SOURCE: Annals of Nuclear Medicine (2001), 15(5), 403-409
CODEN: ANMEEX; ISSN: 0914-7187
PUBLISHER: Japanese Society of Nuclear Medicine
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. Lipid contributes greatly in cardiac metab. to produce high energy ATPs, and is suggested to be related to the progression and deterioration of heart disease. It is fortunate that the I-123-betamethyliodophenylpentadecanoic acid (BMIPP) imaging technique is now available in detg. heart condition, but we must be cautious about the interpretation of images obtained with this new tracer. From the uptake of BMIPP into the cell to breakdown and catabolism of it, there exist so many crit. enzymical pathways relating to the modification of BMIPP imaging. In clin. evaluation, the image will be translated as the integral effects of these pathways. In other words, we must be aware of these crit. pathways regulating lipid metab. and modifying factors in order to correctly understand BMIPP imaging. Lipid transport is affected by the albumin/FFA ratio in the blood, and extn. with membrane transporter proteins. Fatty acid binding protein (FABP) in the cytosole will play an important role in regulating lipid flux and following metab. Lipid will be utilized either for oxidn., triglyceride or phospholipid formation. For oxidn., carnitine palmitoil transferase is the key enzyme for the entrance of lipid into mitochondria, and oxidative enzymes such as acyl CoA dehydrogenase (MCAD, LCAD, HAD) will det. lipid use for the TCA cycle. ATPs produced in the mitochondria again limit the TG store. It is well known that BMIPP imaging completely changes in the ischemic condition, and is also shown that lipid metabolical regulation completely differs from normal in the very early phase of cardiac hypertrophy. .In the process of

deteriorating **heart failure**, metabolical switching of lipid with glucose will take place. In such a different heart disease conditions, it is clear that lipid metabolical regulation, including many lipid enzymes, works differently from in the healthy condition. These lipid enzymes are regulated by nuclear factor peroxisome proliferator-activated receptors (**PPAR**) just like a conductor of an orchestra. Most of the regulating mechanisms of the **PPAR** are still unknown, but redn. of this nuclear factor is shown in the process of decompensated **heart failure**. This review is based by mostly on our fundamental and Japanese clin. data. BMIPP has been used clin. in abundant cases in Japan. In such situations, further correct information on lipid metab., including BMIPP, will contribute to the understanding of deteriorating heart disease and its prognosis.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 26 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:383675 HCAPLUS
DOCUMENT NUMBER: 136:111904
TITLE: Heat-shock proteins: New keys to the development of cytoprotective therapies
AUTHOR(S): Tytell, Michael; Hooper, Philip L.
CORPORATE SOURCE: Department of Neurobiology and Anatomy, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA
SOURCE: Emerging Therapeutic Targets (2001), 5(2), 267-287
CODEN: ETTAF7; ISSN: 1460-0412
PUBLISHER: Ashley Publications Ltd.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review. All cells, from bacterial to human, have a common, intricate response to stress that protects them from injury. Heat-shock proteins (Hsps), also known as stress proteins and mol. chaperones, play a central role in protecting cellular homeostatic processes from environmental and physiol. insult by preserving the structure of normal proteins and repairing or removing damaged ones. An understanding of the interplay between Hsps and cell stress tolerance will provide new tools for treatment and drug design that maximize the preservation or restoration of health. For example, the increased vulnerability of tissues to injury in some conditions, such as ageing, diabetes mellitus, and menopause, or with the use of certain drugs,, such as some antihypertensive medications, is assocd. with an impaired Hsp response. Addnl., diseases that are assocd. with tissue oxidn., free radical formation, disorders of protein folding, or inflammation, may be improved therapeutically by elevated expression of Hsps. The accumulation of Hsps, whether induced physiol., pharmacol., genetically, or by direct administration of the proteins, is known to protect the organism from a great variety of pathol. conditions, including myocardial infarction, stroke, sepsis, viral infection, trauma, neurodegenerative diseases, retinal damage, congestive **heart failure**, arthritis, sunburn, colitis, gastric ulcer, diabetic complications, and transplanted organ failure. Conversely, lowering Hsps in cancer tissues can amplify the effectiveness of chemo- or radiotherapy. Treatments and agents that induce Hsps include hyperthermia, heavy metals (zinc and tin), salicylates, dexamethasone, cocaine, nicotine, alc., α-adrenergic agonists, **PPAR**-γ agonists, Bimoclomol, Geldanamycin, geranylgeranylacetone, and cyclopentenone prostanoids. Compds. that suppress Hsps include quercetin (a bioflavonoid), 15-deoxyspergualin (an immunosuppressive agent), and retinoic acid. Researchers who are

cognizant of the Hsp-related effects of these and other agents will be able to use them to develop new therapeutic paradigms.

REFERENCE COUNT: 201 THERE ARE 201 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 27 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2001:219743 HCAPLUS
DOCUMENT NUMBER: 134:351023
TITLE: **PPAR** Signaling in the Control of Cardiac Energy Metabolism
AUTHOR(S): Barger, P. M.; Kelly, D. P.
CORPORATE SOURCE: Departments of Medicine, Pediatrics, and Molecular Biology & Pharmacology, Center for Cardiovascular Research, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Trends in Cardiovascular Medicine (2001), Volume Date 2000, 10(6), 238-245
CODEN: TCMDEQ; ISSN: 1050-1738
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review, with 75 refs. Cardiac energy metabolic shifts occur as a normal response to diverse physiol. and dietary conditions and as a component of the pathophysiol. processes which accompany cardiac hypertrophy, **heart failure**, and myocardial ischemia. The capacity to produce energy via the utilization of fats by the mammalian postnatal heart is controlled in part at the level of expression of nuclear genes encoding enzymes involved in mitochondrial fatty acid β-oxidn. (FAO). The principal transcriptional regulator of FAO enzyme genes is the peroxisome proliferator-activated receptor α (**PPAR**α), a member of the ligand-activated nuclear receptor superfamily. Among the ligand activators of **PPAR**α are long-chain fatty acids; therefore, increased uptake of fatty acid substrate into the cardiac myocyte induces a transcriptional response leading to increased expression of FAO enzymes. **PPAR**α-mediated control of cardiac metabolic gene expression is activated during postnatal development, short-term starvation, and in response to exercise training. In contrast, certain pathophysiol. states, such as pressure overload-induced hypertrophy, result in deactivation of **PPAR**α and subsequent dysregulation of FAO enzyme gene expression, which sets the stage for abnormalities in cardiac lipid homeostasis and energy prodn., some of which are influenced by gender. Thus, **PPAR**α not only serves a crit. role in normal cardiac metabolic homeostasis, but alterations in **PPAR**α signaling likely contribute to the pathogenesis of a variety of disease states. **PPAR**α as a ligand-activated transcription factor is a potential target for the development of new therapeutic strategies aimed at the prevention of pathol. cardiac remodeling.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 28 OF 28 HCAPLUS COPYRIGHT 2005 ACS on STN

Full Text | Citing References

ACCESSION NUMBER: 2000:601632 HCAPLUS
DOCUMENT NUMBER: 134:125379
TITLE: Rosiglitazone: an agent from the thiazolidinedione

class for the treatment of type 2 diabetes

AUTHOR(S): Cheng-Lai, Angela; Levine, Anne
CORPORATE SOURCE: Department of Pharmacy, Montefiore Medical Center, Bronx, NY, USA

SOURCE: Heart Disease (2000), 2(4), 326-333
CODEN: HTDSFE; ISSN: 1521-737X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; **General Review**
LANGUAGE: English

AB A review with 35 refs. Great advances have been made in the management of diabetes during the past decade. Whereas only one class of oral medications (the sulfonylureas) was available for the treatment of type 2 diabetes in the early 1990s, we now have five classes of oral antidiabetic agents from which to choose. The thiazolidinedione class of medications was first introduced to the United States when troglitazone was marketed during early 1997. Rosiglitazone, approved by the FDA during the spring of 1999, was the second thiazolidinedione to be marketed in the United States. Similar to troglitazone, rosiglitazone improves insulin sensitivity in patients with type 2 diabetes by activating peroxisome proliferator-activated receptor-gamma (**PPAR**γ) receptors in adipose tissues, skeletal muscles, and the liver. The efficacy and safety of rosiglitazone therapy in patients with type 2 diabetes have been demonstrated in a no. of clin. studies, which are summarized in this article. Selected characteristics of rosiglitazone are compared with those of pioglitazone-the other thiazolidinedione currently available in the United States. Edema of mild to moderate severity has been reported in approx. 5% of patients treated with rosiglitazone during clin. trials. Therefore, caution must be taken when this agent is administered to patients with **heart failure**. Rosiglitazone has also been assocd. with elevations of total, LDL, and HDL cholesterol during clin. trials. However, the LDL:HDL cholesterol ratio or the total:HDL cholesterol ratio has mostly been obsd. to be unchanged. Although liver toxicity has not been obsd. with rosiglitazone during clin. trials, the safety of this drug for long-term usage and in larger patient populations remains to be established in further clin. studies and in postmarketing experience.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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